

an HCV type 3a polypeptide or peptide selected from the region spanning positions 1664 to 1764 of the NS3/NS4 region of HCV type 3a;

an HCV type 4 polypeptide or peptide selected from the region spanning positions 127 to 319 of the Core/E1 region of HCV type 4;

an HCV type 4 polypeptide or peptide selected from the region spanning positions 192 to 319 of the E1 region of HCV type 4;

an HCV type 4 polypeptide or peptide selected from the region spanning positions 2645 to 2757 of the NS5B region of HCV type 4;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 1 to 191 of the Core region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 192 to 319 of the E1 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 1 to 319 of the Core/E1 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 328 to 546 of the E1/E2 region of HCV type 5;

an HCV subtype 5 polypeptide or peptide selected from the region spanning positions 1286 to 1403 of the NS3 region of HCV subtype 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 1646 to 1764 of the NS3/NS4 region of HCV type 5;

an HCV type 5 polypeptide or peptide selected from the region spanning positions 2645 to 2757 of the NS5 region of HCV type 5;

an HCV subtype 2d polypeptide or peptide selected from the region spanning positions 1 to 319 of the Core/E1 region of HCV subtype 2d;

an HCV subtype 2d polypeptide or peptide selected from the region spanning positions 192 to 319 of the E1 region of HCV subtype 2d;

an HCV subtype 2d polypeptide or peptide selected from the region spanning positions 2645 to 2757 of the NS5B region of HCV subtype 2d;

wherein said peptide or polypeptide contains at least one genotype-specific amino acid.

~~57~~

57. (new) An HCV type 5 polypeptide or peptide selected from the region spanning positions 1 to 2757 of HCV type 5, and wherein said peptide or polypeptide is obtainable by amplification of HCV type 5 specific polynucleic acids using HCV type 5 specific primers,

and wherein said peptide or polypeptide contains at least one genotype-specific amino acid.

~~58~~

58. (new) An isolated HCV type 3a polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 14, 16, 18, 20, 22, 24, 26 or 28,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 140 to 319 of the Core/E1 region of HCV type 3a.

59. (new) An isolated HCV type 3a polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 30, 32, 34, 36, 38, or 40,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1646 to 1764 of the NS3/NS4 region of HCV type 3a.

58/60. (new) An isolated HCV type 4 polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 119, 121 or 123,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 127 to 319 of the Core/E1 region of HCV type 4.

59/61. (new) An isolated HCV type 4 polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 119, 121 or 123,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 192 to 319 of the E1 region of HCV type 4.

62. (new) An isolated HCV type 4 polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 106, 108, 110, 112, 114 or 116,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 2645 to 2757 of the NS5B region of HCV type 4.

63. (new) An isolated HCV type 4 polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 164 or 166,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 319 of the Core/E1 region of HCV type 4.

64. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 42, 44, 46, 48, 50, 52, 54, or 152,

(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 191 of the Core region of HCV type 5.

65. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 42, 44, 46, 48, 50, 52, or 54,  
(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 192 to 319 of the E1 region of HCV type 5.

66. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

(i) the polypeptides or peptides of SEQ ID NO: 42, 44, 46, 48, 50, 52, 54, 154 or 156,  
(ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 319 of the Core/E1 region of HCV type 5.

~~67~~ 67. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

- C1  
cont.
- (i) the polypeptide or peptide of SEQ ID NO: 158,
  - (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 328 to 546 of the Core/E1 region of HCV type 5.

~~68~~ 68. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 56, or 58,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1286 to 1403 of the NS3 region of HCV type 5.

~~69~~ 69. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 60, or 62,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1646 to 1746 of the NS3/NS4 region of HCV type 5.

*C1*  
*CONT.*  
~~70~~  
70. (new) An isolated HCV type 5 polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 160 or 162,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 2645 to 2757 of the NS5 region of HCV type 5.

~~71~~  
71. (new) An isolated HCV subtype 2d polypeptide or peptide selected from the group consisting of

- (i) the polypeptides or peptides of SEQ ID NO: 144,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 1 to 319 of the Core/E1 region of HCV subtype 2d.

~~72~~  
72. (new) An isolated HCV subtype 2d polypeptide or peptide selected from the group consisting of

- (i) the polypeptide or peptide of SEQ ID NO: 144,
- (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 192 to 319 of the E1 region of HCV subtype 2d.

~~73~~  
73. (new) An isolated HCV subtype 2d polypeptide or peptide selected from the group consisting of

- C1  
CONT
- (i) the polypeptide or peptide of SEQ ID NO: 146,
  - (ii) at least 5 amino acids from the polypeptide or peptide of (i) having at least one genotype-specific amino acid from the region spanning positions 2645 to 2757 of the NS5B region of HCV subtype 2d.

~~74~~  
74. An isolated HCV polypeptide or peptide according to any of claims ~~56 or 57~~, which contains in its sequence at least one of the following amino acid residues:

SUB D3

L7, M44, R67, Q70, A79, A87, N106, K115, A127, A190, S130, V134, G142, 1144, E152, A157, V158, P165, S177 or Y177, 1178, V180 or E180 or F182, R184, 1186, H187, T189, A190, S191 or G191, Q192 or L192 or 1192 or V192 or E192, N193 or H193 or P193, W194 or Y194, H195, A197 or 1197 or V197 or T197, V202, 1203 or L203, Q208, A210, V212, F214, T216, R217 or D217 or E217 or V217, H218 or N218, H219 or V219 or L219, L227 or 1227, M231 or E231 or Q231, T232 or D232 or A232 or K232, Q235 or 1235, A237 or T237, 1242, 1246, S247, S248, V249, S250 or Y250, 1251 or V251 or M251 or F251, D252, T254 or V254, L255 or V255, E256 or A256, M258 or F258 or V258, A260 or Q260 or S260, A261, T264 or Y264, M265, 1266 or A266, A267, G268 or T268, F271 or M271 or V271, 1277, M280 or H280, 1284 or A284 or L84, V274, V291, N292 or S292, R293 or 1293 or Y293, Q294 or R294, L297 or 1297 or Q297, A299 or K299 or Q299, N303 or T303, T308 or L308, T310 or F310 or A310 or D310 or V310, L313, G317 or Q317, L333, S351, A358, A359, A363, S364,



MAERTENS t al.  
Serial N . 09/638,693

C1  
DNT  
SUB D3  
Cont

A366, T369, L373, F376, Q386, 1387, S392, 1399, F402, 1403, R405, D454, A461,  
A463, T464, K484, Q500, E501, S521, K522, H524, N528, S531, S532, V534, F536,  
F537, M539, 1546, C1282, A1283, H1310, V1312, Q1321, P1368, V1372, V1373,  
K1405, Q1406, S1409, A1424, A1429, C1435, S1436, S1456, H1496, A1504, D1510,  
D1529, 11543, N1567, D1556, N1567, M1572, Q1579, L1581, S1583, F1585, V1595,  
E1606 or T1606, M1611, V1612 or L1612, P1630, C1636, P1651, T1656 or 11656,  
L1663, V1667, V1677, A1681, H1685, E1687, G1689, V1695, A1700, Q1704, Y1705,  
A1713, A1714 or S1714, M1718, D1719, A1721 or T1721, R1722, A1723 or V1723,  
H1726 or G1726, E1730, V1732, F1735, 11736, S1737, R1738, T1739, G1740, Q1741,  
K1742, Q1743, A1744, T1745, L1746, E1747 or K1747, 11749, A1750, T1751 or  
A1751, V1753, N1755, K1756, A1757, P1758, A1759, H1762, T1763, Y1764, P2645,  
A2647, K2650, K2653 or L2653, S2664, N2673, F2680, K2681, L2686, H2692, Q2695  
or L2695 or 12695, V2712, F2715, V2719 or Q2719, T2722, T2724, S2725, R2726,  
G2729, Y2735, H2739, 12748, G2746 or 12746, 12748, P2752 or K2752, P2754 or  
T2754, T2757 or P2757.

75 ~~75~~  
75. (new) A polypeptide or peptide according to any of claims 56 or 57, wherein  
said polypeptide or peptide is selected from the following peptides:

QPTGRSWGQ (SEQ ID NO 93)  
RSEGRTSWAQ (SEQ ID NO 220)  
RTEGRTSWAQ (SEQ ID NO 221)  
LEWRNTSGLYVL (SEQ ID NO 83)

C1  
CONT.

SUB D3  
CONT.

VNYRNASGIYHI	(SEQ ID NO 126)
QHYRNISGIYHV	(SEQ ID NO 127)
EHYRNASGIYHI	(SEQ ID NO 128)
IHYRNASGIYHI	(SEQ ID NO 224)
VPYRNASGIYHV	(SEQ ID NO 84)
VNYRNASGIYHI	(SEQ ID NO 225)
VNYRNASGVYHI	(SEQ ID NO 226)
VNYHNTSGIYHL	(SEQ ID NO 227)
QHYRNASGIYHV	(SEQ ID NO 228)
QHYRNVSGIYHV	(SEQ ID NO 229)
IHYRNASDGYI	(SEQ ID NO 230)
LQVKNTSSSYMV	(SEQ ID NO 231)
VYEADDVILHT	(SEQ ID NO 85)
VYETEHILHL	(SEQ ID NO 129)
VYEADRHIMEL	(SEQ ID NO 130)
VYETDHHILHL	(SEQ ID NO 131)
VYEADNLILHA	(SEQ ID NO 86)
VWQLRAIVLHV	(SEQ ID NO 232)
VYEADYHILHL	(SEQ ID NO 233)
VYETDNHILHL	(SEQ ID NO 234)
VYETENHILHL	(SEQ ID NO 235)
VFETVHH1LHL	(SEQ ID NO 236)

MAERTENS et al.  
S rial No. 09/638,693

VFETEHHLHL	(SEQ ID NO 237)
VFETDHHIMHL	(SEQ ID NO 238)
VYETENHILHL	(SEQ ID NO 239)
VYEADALILHA	(SEQ ID NO 240)
VQDGNTSTCWTPV	(SEQ ID NO 87)
VQDGNTSACWTPV	(SEQ ID NO 241)
VRVGNQSRCWVAL	(SEQ ID NO 132)
VRTGNTSRCWVPL	(SEQ ID NO 133)
VRAGNVSRCWTPV	(SEQ ID NO 134)
EEKGNISRCWIPV	(SEQ ID NO 242)
VKTGNQSRCWVAL	(SEQ ID NO 243)
VRTGNQSRCWVAL	(SEQ ID NO 244)
VKTGNQSRCWIAL	(SEQ ID NO 245)
VKTGNVSRWVPL	(SEQ ID NO 247)
VKTGNVSRWVSL	(SEQ ID NO 248)
VRKDNVSRWVQI	(SEQ ID NO 249)
VRVVGATTAS	(SEQ ID NO 89)
APYIGAPLES	(SEQ ID NO 135)
APYVGAPLES	(SEQ ID NO 136)
AVSMDAPLES	(SEQ ID NO 137)
APSLGAVTAP	(SEQ ID NO 90)
APSFGAVTAP	(SEQ ID NO 250)

VSQPGALTKG	(SEQ ID NO 251)
VKYVGATTAS	(SEQ ID NO 252)
APYIGAPVES	(SEQ ID NO 253)
AQHNLAPLES	(SEQ ID NO 254)
SPYVGAPLEP	(SEQ ID NO 255)
SPYAGAPLEP	(SEQ ID NO 256)
APYLGAPLEP	(SEQ ID NO 257)
APYLGAPLES	(SEQ ID NO 258)
APYVGAPLES	(SEQ ID NO 259)
VPYLGAPLTS	(SEQ ID NO 260)
APHLRAPLSS	(SEQ ID NO 261)
APYLGAPLTS	(SEQ ID NO 262)
RPRRHQTVQT	(SEQ ID NO 91)
QPRRHWTQD	(SEQ ID NO 138)
RPRRHWTQD	(SEQ ID NO 139)
RPRQHATVQN	(SEQ ID NO 92)
RPRQHATVQD	(SEQ ID NO 263)
SPQH HKFVQD	(SEQ ID NO 264)
RPRRLWTTQE	(SEQ ID NO 265)
PPRIHETTQD	(SEQ ID NO 266)
TISYANGSGPSDDK	(SEQ ID NO 267)

C1  
CONT

SUB D3  
cont

Sub  
1A7  
76. (new) A composition comprising an isolated polypeptide or peptide according  
54 56 57  
to any of claims ~~56 or 57~~.

77. (new) A method for raising antibodies comprising the use of a polypeptide or  
56 54 02 55 57  
peptide according to any of claims ~~56 or 57~~.

78. (new) A method of detecting, screening or confirmation for the presence of  
HCV antibodies present in a biological sample, comprising the following steps:

- (i) providing a sample suspected of containing HCV antibody,
- (ii) contacting the sample with a polypeptide or peptide according to  
56 54 02 55 57  
any of claims ~~56 or 57~~, under appropriate conditions allowing the formation of an  
immune complex,
- (iii) inferring from the presence of the immune complex of step (ii) the  
presence of HCV antibodies in said sample.

79  
79. (new) A method of detecting, screening or confirmation for one or more HCV  
serotypes present in a biological sample, comprising the following steps:

- (i) providing a sample suspected of containing HCV antibody,
- (ii) contacting the sample with a polypeptide or peptide according to any of  
56 54 02 55 57  
claims ~~56 or 57~~, under appropriate conditions allowing the formation of an immune  
complex,

(iii) inferring from the presence of one or more of these immune complexes of step (ii) the serotype(s) present in said sample.

80. (new) A method for detecting HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following steps:

(i) contacting the biological sample to be analyzed for the presence of HCV antibodies with at least one peptide or polypeptide according to any of

claims ~~56 or 57~~ <sup>56 or 57</sup>, preferentially in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide or peptide is preferentially in the form of a biotinylated polypeptide or peptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes,

(ii) removing unbound components,

(iii) incubating the immune complexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,

(iv) detecting the presence of said immune complexes visually or by means of densitometry and inferring the HCV serotype(s) present from the observed binding pattern.

~~81~~

81. (new) A method for confirmation of HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following steps:

(i) contacting the biological sample to be analyzed for the presence of HCV antibodies with at least one peptide or polypeptide according to any of claims ~~56~~ or 57, preferentially in an immobilized form under appropriate conditions which allow the formation of an immune complex, wherein said polypeptide or peptide is preferentially in the form of a biotinylated polypeptide or peptide and is covalently bound to a solid substrate by means of streptavidin or avidin complexes,

(ii) removing unbound components,

(iii) incubating the immune complexes formed with heterologous antibodies, which specifically bind to the antibodies present in the sample to be analyzed, with said heterologous antibodies having conjugated to a detectable label under appropriate conditions,

(iv) detecting the presence of said immune complexes visually or by means of densitometry and confirm the HCV serotype(s) present from the observed binding pattern.

~~82~~

82. (new) A kit for detecting, screening or confirmation for one or more HCV serotype(s) present in a biological sample, comprising:

(i) a polypeptide or peptide according to any of claims ~~56~~ or 57,

~~56~~ or ~~57~~

(ii) possibly a buffer and components necessary for producing the formation of an immune complex,

(iii) possibly a means for detecting, screening or confirming the immune complex(es) formed.

83. (new) A kit for detecting, screening or confirmation for the presence of HCV antibodies present in a biological sample, comprising the following steps:

(i) a polypeptide or peptide according to any of claims ~~56 or 57~~, <sup>56 57</sup>

(ii) possibly a buffer and components necessary for producing the formation of an immune complex,

(iii) possibly a means for detecting, screening or confirming the immune complex formed.

84. (new) A kit for detecting HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following components:

(i) at least a polypeptide or peptide according to any of claims ~~56 or 57~~, <sup>56 57</sup> with said polypeptide or peptide being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,

(ii) a buffer and components necessary for producing the buffer enabling binding reaction between these polypeptides or peptides and the antibodies against HCV present in the biological sample,



(iii) optionally, a detector for determining the presence of immune complexes formed in the preceding binding reaction, and

(iv) optionally an automated scanning and interpretation device to confirm the HCV serotype(s) present in the sample from the observed binding pattern.

85. (new) A kit for confirmation of HCV serotype(s) present in a biological sample liable to contain it, comprising at least the following components:

(i) at least a polypeptide or peptide according to any of claims 56 or 57, with said polypeptide or peptide being preferentially immobilized on a solid substrate, and more preferentially on one and the same membrane strip,

(ii) a buffer and components necessary for producing the buffer enabling binding reaction between these polypeptides or peptides and the antibodies against HCV present in the biological sample,

(iii) optionally, a detector for determining the presence of immune complexes formed in the preceding binding reaction, and

(iv) optionally, an automated scanning and interpretation device to confirm the HCV serotype(s) present in the sample from the observed binding pattern.--

REMARKS

Reconsideration is requested.